**Development of the Reproductive System**

Transcription Factors & Hormones

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| TDF (Testis-Determining Factor) | REQUIRED for development of phenotypic male. From SRY gene.  **Inhibits** Dax-1.  Causes gonadal cords to condense & form seminiferous tubules. |
| BMP-4 | Controls formation of germ cells in endoderm of yolk sac & migration into medial UG ridge (day 24) |
| LIF & STEEL Factor | Induce proliferation of germ cells in gonad after migration from endoderm of yolk sac |
| Oct-4 | Maintains totopotential state of germ cells (able to grow into any type of cell) |
| Wt-1 & SF-1 | Affects **somatic cells**, NOT germ cells. |
| Lim-1 | Needed for the formation of anterior head, kidneys, & gonads |
| Sry Gene | On the short arm of the Y chromosome 🡪 produces TDF |
| Dax-1 | **Inhibits** testis formation |
| Sox-9 | Causes growth of gonadal cords into mesenchyme |
| Testosterone + Androstenedione | Secreted by fetal Leydig cells 🡪 differentiation of genital **ducts** (9-14 weeks) |
| hCG | Secreted by placenta, indicating pregnancy. Causes peak of testosterone + androstenedione for the differentiation of genital ducts. |
| MIS (Muellerian-Inhibiting Substance) | Secreted by Sertoli cells 🡪 involution of the female ducts (**paramesonephric ducts degenerate**)  If testis don’t form properly, can’t secrete MIS. Thus, can be XY with female ducts. |
| MIF (Meiosis-Inhibiting Factor) | Secreted by Sertoli cells 🡪 Slows growth of primordial germ cells |
| MSF (Meiosis Stimulating Factor) | Induces oogonia to enter meiosis. From mesonephric tubule cells associated with rete ovarii. |
| Testosterone | Secreted by Leydig cells.  Induces distal mesonephric duct to be highly convoluted 🡪 epididymis, vas deferens, ejaculatory duct, & seminal vesicles.  UG Sinus development.  Descent of testis in all 3 phases (Initial, Transabdominal, & Transinguinal) |
| Hoxa-10 & 11 | Form epididymis |
| Hoxd-11, 12, 13 | Form vas deferens |
| Hoxd-13 | **Determines where the prostate gland develops**.  Induces budding of endoderm (testosterone-induced mesenchyme below bladder) for **prostate gland** |
| Wnt-4 | Necessary for **Paramesonephric Duct** development. |
| Wnt-7a | Necessary for Hoxd 10-13 expression. |
| Hox, BMP-4, ssh + FGF-4 | Necessary for external genitalia formation. |
| Ssh, FGF-8 + FGF-10 | Necessary for outgrowth of genital tubercle (from genital eminence). |
| Testosterone + Dihydrotestosterone | Secreted by Leydig cells 🡪 influences male external genitalia |
| Insl-3 | Required for Transabdominal Descent of Testis (Part 2 of Descent).  If absent = **Bilateral cryptochidism** |

Male vs. Female Structure & Precursor

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| **Male** | Spermatogonia | Primordial germ cells |
| Sertoli cells | Mesenchyme |
| Seminiferous tubules | Outer portion of gonadal cords |
| Straight tubules & Rete testis | Inner portion of gonadal cords |
| Efferent ductules | Mesonephric tubules |
| Leydig Cells | Mesenchyme |
| Prostatic Utricle | Remnant of paramesonephric duct |
| Appendix to Testis | Remnant of paramesonephric duct |
| Bladder | Vesical portion of UG sinus |
| Membranous & Prostatic Urethra | Pelvic portion of UG sinus |
| Penile Urethra | Phallic portion of UG sinus |
| Prostate Gland | Outgrowth of endoderm (testosterone-induced mesenchyme) just below bladder |
| Bulbourethral glands & Glands of Littre | Endodermal-derived *Penile Urethra* |
| Fossa Navicularis | Ectoderm plate |
| Penile Urethra | Fusion of urogenital folds posterior to anterior.  UG sinus **endoderm** with surface ectoderm covering the closure. |
| Penile Raphe | Forms where the fusion of the genital folds occurs. **Ectoderm covering**. |
| Prepuce/Foreskin | Circular ingrowth of **ectoderm** around glans of penis. |
| Corpora Cavernosa & Spongiosa | **Mesenchyme** of the phallus. **Mesoderm**. |
| Scrotum | From the fusion of the labialscrotal swellings at the midline. |
| Scrotal Raphe | Fusion line between the labialscrotal swellings. |
| Tunica Vaginalis | Remnant of degenerated processus vaginalis.  Double layer that encases the testis. |
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| **Female** | Oogonia | Primordial germ cells |
| Follicular cells | **Cortical** **cords** from mesothelium & mesenchyme from mesonephric tubules.  Surface epithelium of the ovary. |
| Stroma cells | Mesenchyme surrounding the primordial follicles. |
| Primordial follicles | Cords break into small clusters with oogonia. |
| Uterine Tubes | Cranial portion of paramesonephric ducts |
| Uterovaginal Primordium  (Uterus & Superior Vagina) | Fusion of the two Muellerian ducts (Paramesonephric ducts) |
| Broad Ligament | Movement of paramesonephric ducts towards the midline. |
| Rectouterine & Vesicouterine Pouches | Movement of paramesonephric ducts towards the midline. |
| Uterus | Superior part of paramesonephric ducts that fuse together as a solid cord. Wall degenerates to form lumen. |
| Superior Vagina | Inferior part of paramesonephric ducts that fuse together as a solid cord. |
| Vagina | Vaginal plate from the fusion of the **sinovaginal bulbs**. Central cells break for form lumen. |
| Hymen | Membrane that separates the vaginal opening from the vestibule. |
| Greater Vestibular Glands | Outpocketings of the UG sinus **endoderm**. |
| Hydatid (of Morgagni) | Remnant of paramesonephric ducts adjacent to infundibulum.  (The only paramesonephric duct remnant). |
| Remnants of **Mesonephric Ducts** | 1. Appendix of Vesiculosa 2. Epoophron (efferent ductules/epididymis) 3. Paraoophoron 4. Gartner Duct Cysts |
| Clitoris | Primordal phallus. Urethra *not* incorporated b/c UG folds don’t fuse. |
| Labia Minora | Unfused UG folds. |
| Labia Majora | Unfused Labialscrotal Swellings |
| Mons Pubis | Labialscrotal Swellings. |
| Vestibule of Vagina | Phallic portion of UG sinus. |

**Abnormalities of Sexual Differentiation**

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| **True Hermaphrodites** | **Female Pseudohermaphrodites** | **Male Pseudohermaphrodites** |
| Barr Bodies | Barr Bodies | NO Barr Bodies |
| 70% 46, XX  20% Mosaics  10% 46, XY | 46, XX | 46, XY |
| BOTH Ovarian & Testicular Tissue\* | Ovaries | Testes |
| **Phenotype**: Ambiguous genitalia, enlarged clitoris, partially fused labia, amenorrhea | **Phenotype:** Enlarged clitoris, fused labia, persistent UG sinus, possible clitoral urethra (“small penis”) | **Phenotype**: Variable external genitalia (\*See AIS), hypoplasia of phallus, paramesonephric ducts (due to low MIS) |
| **Cause**: Errors in sex determination | **Cause**: Excessive androgens = **CAH** (Congenital Adrenal Hyperplasia) | **Cause**: Low levels of testosterone & MIS (Defective Leydig cells or receptors) |
| \***Androgen Insensitivity Syndrome (AIS)**: female external genitalia; vagina = blind pouch; absent or primitive uterus/tubes; **estrogen** for 2° sex characteristics via androgen-converting adrenal cortex; no menstruation; testis in abdomen/inguinal canal; NO Barr Bodies; testis still secrete MIS 🡪 **no duct system**; testis removed to reduce risk of tumors  **Cause**: Defect in androgen receptors in genital tubercle, UG folds, & labialscrotal swellings. Socially reared as women. |